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Robin M. Silva, Esq.
FLEHR HOHBACH TEST ALBRITTON & HERBERT LLP
Suite 3400
Four Embarcadero Center
San Francisco, CA 94111-4187

EXAMINER

LU, FRANK WEI MIN

ART UNIT

PAPER NUMBER

1634

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/779,376

Applicant(s)

FAN ET AL.

Examiner

Frank Lu

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 28 March 2002.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 5,9-16 and 19-23 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 5,9-16 and 19-23 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) ☐ Interview Summary (PTO-413) Paper No(s) _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☒ Other: *Detailed Action*.

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Election/Restriction

1. Applicant's election without traverse of Groups II, claims 5, 9-16, 19-23, and 26 in Paper No. 8 is acknowledged.

Oath/Declaration

2. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because the inventor, Jian-Bing Fan, did not sign his full name (family name and at least one given name together with any initial).

Specification

3. The disclosure is objected to because of the following informalities: (1) The Brief Descriptions of the Drawings 1-6 do not comply with 37 CFR 1.74. Specifically, a separate reference to and brief description of each of the drawings must be present in the disclosure; (2) although there is an item 30 in Figure 7, there is no description of item 30 in The Brief Description of the Drawing 7; (3) although The Brief Descriptions of the Drawings 8-10 describe "detection position 10", there is no item 10 in Figures 8-10; and (4) although The Brief Description of the Drawing 10 describes "upstream universal priming site 25", there is no item 25 in Figure 10.

Appropriate correction is required.

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Claim Objections

4. Claims 19-21 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim since claim 26 requires that the target sequence immobilizes on a support. Note that claims 19-21 are dependent on claim 26.

Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

5. Claims 5 and 26 are objected to because of the following informalities: (1) a coma should be added between "said detection position" and "a ligation complex" in step b); and (2) "and" should be deleted between "a ligation complex is formed" and "wherein" in step b).

6. Claim 9 is objected to because of the following informality: "said probe" in step d) should be "said probes".

Appropriate correction is required.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 9-12, 22, and 23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Note that claim 11 is dependent on claim 10 while claim 12 is dependent on claim 9.

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9. Claim 9 is rejected as vague and indefinite over the steps a) and b) of the claim because it is unclear how said target sequence in step (a) corresponds to said target sequence in step b) since said target sequence in step a) does not have said binding ligand while target sequence in step b) comprises said binding ligand? Please clarify.
10. Claim 10 is rejected as vague and indefinite because it is unclear how said removing can be done using a double-stranded specific moiety? Please clarify.
11. Claim 22 is rejected as vague and indefinite over "wherein said target sequence is attached to said support by a method selected from the group consisting of labeling said target sequence with a functional attachment moiety" because "labeling said target sequence with a functional attachment moiety" is not an attachment method. Please clarify.
12. Claim 23 recites the limitation "said support" in the claim. There is insufficient antecedent basis for this limitation in the claim since there is no support in claim 5.

Claim Rejections - 35 USC § 102

13. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(e) the invention was described in-

(1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or

(2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes

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of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

14. Claims 5 and 13 are rejected under 35 U.S.C. 102(e) as being anticipated by Barany *et al.*, (US Patent No. 6,027,889, filed on May 28, 1997).

Barany *et al.*, teach detection of nucleic acid sequence differences using coupled ligase detection and polymerase chain reactions. As shown in Figures 12-17, a first oligonucleotide probe having a target-specific portion and a 5' upstream primer-specific portion, and a second oligonucleotide probe having a target-specific portion and a 3' downstream primer-specific portion were hybridized adjacent to one another on a corresponding target nucleotide sequence and were ligated together in a ligase chain reaction. However, if there was a mismatch in ligation end of the first or second probe, this mismatch would interfere with such ligation. Then unligated the first probe and the second probe were removed with Exo I and PCR-amplified using an upstream primer containing the same sequence as the 5' upstream primer-specific portion of the ligation product sequence (in the first probe) and a downstream primer complementary to the 3' downstream primer-specific portion of the ligation product sequence (in the second probe) wherein one primer had a detectable reporter label. Finally, PCR products were hybridized with a DNA array with different capture oligonucleotides immobilized at different particular sites and had nucleotide sequences complementary to the unique nucleotide sequences across the ligation junctions of given probe sets, and the labels of the PCR products captured on the DNA array at particular sites were detected as recited in steps f) and g) of claim 5 (see Figures 12-17 and columns 9, 10, 25-28, and 79-90). Note that: (1) the first probe and second probe was considered as first and second ligation probe as recited in claim 5; (2) 5' upstream primer-specific

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portion in the first probe and 3' downstream primer-specific portion in the second probe were considered as UUP and DUP or an adaptor sequence as recited in claim 5; (3) since claim 5 does not require that step c) must perform before step d), Exo I digestion step was considered as step c) recited in claim 5; and (4) claim 13 was considered as basic PCR steps including repeated denaturation, annealing and extension.

Therefore, Barany *et al.*, teach all limitations recited in claims 5 and 13.

Claim Rejections - 35 USC § 103

15. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

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16. Claims 14-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Barany *et al.*, (1997) as applied to claims 5 and 13 above, and further in view of Walt *et al.*, (US Patent No. 6,327,410 B1, filed on September 11, 1998).

The teachings of Barany *et al.*, have been summarized previously, *supra*.

Barany *et al.*, did not disclose an array recited in claims 14-16.

Walt *et al.*, do teach an array comprising a substrate such as a fiber optical bundle recited in claim 16 with a patterned surface with discrete sites such as wells recited in claim 15 and a population of microspheres comprising at least a first subpopulation and a second subpopulation wherein said first subpopulation comprises a first nucleic acid and second subpopulation comprises a second nucleic acid, and wherein said microspheres are randomly distributed on said surface such that said discrete sites contain microspheres recited in claim 14 (see Figures 7A and 7B, columns 3, 4, and 28-30).

Therefore, in the absence of an unexpected result, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have performed the method recited in claim 5 using an array recited in claims 14-16 in view of the patents of Barany *et al.*, and Walt *et al.*. One having ordinary skill in the art would have been motivated to modify the method of Barany *et al.*, because the simple replacement of one kind of nucleic acid array (a regular oligonucleotide array) from another kind of nucleic acid array (an array with microspheres having immobilized nucleic acids) would have been, in the absence of an unexpected result, *prima facie* obvious to one having ordinary skill in the art at the time the invention was made.

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Furthermore, the motivation to make the substitution cited above arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making the obviousness rejection comes from the M.P.E.P. at 2144.07 and 2144.09.

Also note that there is no invention involved in combining old elements in such a manner that these elements perform in combination the same function as set forth in the prior art without giving unobvious or unexpected results. *In re Rose* 220 F.2d. 459, 105 USPQ 237 (CCPA 1955).

17. Claims 13, 19-23, and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zhang *et al.*, (US Patent No. 5,876,924, filed on July 31, 1996) in view of Barany *et al.*, (1997) and in light of Seradyn Particle Technology (November 1996).

Regrading claims 13, 19-23, and 26, Zhang *et al.*, teach nucleic acid amplification method hybridization signal amplification method. As shown in Figures 1 and 2, the two oligonucleotide probes (Capture/Amp-probe-1 and Amp-probe-2) were first hybridized adjacent to one another on a corresponding target nucleotide sequence of the target nucleic acid in a sample wherein the Capture/Amp-probe-1 was 3'-biotinylated. Then the complex comprising target nucleic acid-probes was separated from any unbound reactants using streptavidin-coated paramagnetic beads as recited in claims 19 and 20 and the probes were ligated together in a ligation chain reaction. Ligated product of Capture/Amp-probe-1 and Amp-probe-2 were used as a template for PCR (see Figures 1 and 2, and columns 10-17). Note that: (1) since claim 26 does not require that step a) must perform before step b), binding of target nucleic acid-probe complex

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to streptavidin-coated paramagnetic beads could be considered to provide a support on which the target sequence was immobilized recited in step a) of claim 26; (2) (d) domain of Capture/Amp-probe-1 and (g) domain of AMP-PROBE-2 were considered as DUP and UUP or adaptor sequences respectively; (3) the target nucleic acid was considered to be indirectly immobilized on streptavidin-coated paramagnetic beads as recited in claims 19 and 21; (4) biotinylated Capture/Amp-probe-1 could be considered as a functional attachment moiety recited in claim 22 since this probe attached the target nucleic acid to streptavidin-coated paramagnetic beads in the target nucleic acid-probe complex; and (5) streptavidin-coated paramagnetic beads could be considered to be made by plastic since these beads could have polystyrene core (see Seradyn Particle Technology, page 7).

Zhang *et al.*, did not disclose steps g) and h) of claim 26.

The teachings of Barany *et al.*, have been summarized previously, *supra*. Barany *et al.*, also teach steps g) and h) of claim 26 (see above).

Therefore, in the absence of an unexpected result, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have performed the method recited in claim 26 using a PCR product made by Zhang *et al.*, as a hybridization probe in view of the patents of Barany *et al.*, and Zhang *et al.*. One having ordinary skill in the art would have been motivated to modify the method of Barany *et al.*, because the simple replacement of one well known LDR/PCR method (the method of Barany *et al.*,) from another well known LDR/PCR method (the method of Zhang *et al.*,) in order to make a

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hybridization probe would have been, in the absence of an unexpected result, *prima facie* obvious to one having ordinary skill in the art at the time the invention was made.

Furthermore, the motivation to make the substitution cited above arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making the obviousness rejection comes from the M.P.E.P. at 2144.07 and 2144.09.

Also note that there is no invention involved in combining old elements in such a manner that these elements perform in combination the same function as set forth in the prior art without giving unobvious or unexpected results. *In re Rose* 220 F.2d. 459, 105 USPQ 237 (CCPA 1955).

Conclusion

17. No claim is allowed.

18. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CAR § 1.6(d)). The CM Fax Center number is either (703) 308-4242 or (703)305-3014.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Lu, Ph.D., whose telephone number is (703) 305-1270. The examiner can normally be reached on Monday-Friday from 9 A.M. to 5 P.M.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached on (703) 308-1152.

Any inquiry of a general nature or relating to the status of this application should be directed to the patent Analyst of the Art Unit, Ms.Chantae Dessau, whose telephone number is (703) 605-1237.

A handwritten signature in cursive script, appearing to read "Frank Lu".

Frank Lu
May 6, 2002